Contents of Volume 62

January 1998

i **This Month in the *Journal***
John Ashkenas

Immunogenetics '98

1 **HLA and Pregnancy: The Paradox of the Fetal Allograft**
Carole Ober

6 **Genetic Heterogeneity of Mannose-Binding Proteins: The Jekyll and Hyde of Innate Immunity?**
R. Alan B. Ezekowitz

Insights from Model Systems

10 ***Drosophila* Immune Responses as Models for Human Immunity**
Mitchell S. Dushay and Elizabeth D. Eldon

Invited Editorials

15 **Mitochondrial Mutations and Hearing Loss: Paradigm for Mitochondrial Genetics**
Nathan Fischel-Ghodsian

20 **Paraoxonase-Gene Polymorphisms Associated with Coronary Heart Disease: Support for the Oxidative Damage Hypothesis?**
Jay W. Heinecke and Aldons J. Lusis

25 **One Fewer Worry for Survivors of Childhood Cancer**
J. M. Friedman

Original Articles

27 **Familial Progressive Sensorineural Deafness Is Mainly Due to the mtDNA A1555G Mutation and Is Enhanced by Treatment with Aminoglycosides**
Xavier Estivill, Nancy Govea, Anna Barceló, Enric Perelló, Cèlia Badenas, Enrique Romero, Luis Moral, Rosaria Scozzari, Leila D'Urbano, Massimo Zeviani, and Antonio Torroni

36 **DNA Polymorphisms in Two Paraoxonase Genes (PON1 and PON2) Are Associated with the Risk of Coronary Heart Disease**
Dharambir K. Sanghera, Christopher E. Aston, Nilmani Saha, and M. Ilyas Kamboh

45 **Genetic Disease in Offspring of Long-Term Survivors of Childhood and Adolescent Cancer**
Julianne Byrne, Sonja A. Rasmussen, Sandra C. Steinhorn, Roger R. Connelly, Max H. Myers, Charles F. Lynch, John Flannery, Donald F. Austin, Frederick F. Holmes, Grace E. Holmes, Louise C. Strong, and John J. Mulvihill

53 **Genotype-Phenotype Correspondence in Sanfilippo Syndrome Type B**
Hong G. Zhao, Elena L. Aronovich, and Chester B. Whitley

64 ***NAGLU* Mutations Underlying Sanfilippo Syndrome Type B**
Artur Schmidtchen, David Greenberg, Hong G. Zhao, Hong Hua Li, Yan Huang, Phuong Tieu, Hui-Zhi Zhao, Samson Cheng, Zhaoyang Zhao, Chester B. Whitley, Paola Di Natale, and Elizabeth F. Neufeld

70 **A Presenilin-1 Truncating Mutation Is Present in Two Cases with Autopsy-Confirmed Early-Onset Alzheimer Disease**
Carolyn Tysoe, Joanne Whittaker, John Xuereb, Nigel J. Cairns, Marc Cruts, Christine Van Broeckhoven, Gordon Wilcock, and David C. Rubinsztein

77 **Molecular Analysis of Mutations in the *CSB* (*ERCC6*) Gene in Patients with Cockayne Syndrome**
Donna L. Mallery, Bianca Tanganelli, Stefano Colella, Herdis Steingrimsdottir, Alain J. van Gool, Christine Troelstra, Miria Stefanini, and Alan R. Lehmann

86 **Ataxia-Telangiectasia: Identification and Detection of Founder-Effect Mutations in the ATM Gene in Ethnic Populations**
Milhan Telatar, Sharon Teraoka, Zhijun Wang, Helen H. Chun, Teresa Liang, Sergi Castellvi-Bel, Nitin Udar, Anne-Lise Borresen-Dale, Luciana Chessa, Eva Bernatowska-Matuszkiewicz, Oscar Porras, Mitsunori Watanabe, Anne Junker, Patrick Concannon, and Richard A. Gatti

98 **Analysis of the COL1A1 and COL1A2 Genes by PCR Amplification and Scanning by Conformation-Sensitive Gel Electrophoresis Identifies Only COL1A1 Mutations in 15 Patients with Osteogenesis Imperfecta Type I: Identification of Common Sequences of Null-Allele Mutations**
Jarmo Körkkö, Leena Ala-Kokko, Anne De Paepe, Lieve Nuytinck, James Earley, and Darwin J. Prockop[1]

111 **The GAA Triplet-Repeat Expansion in Friedreich Ataxia Interferes with Transcription and May Be Associated with an Unusual DNA Structure**
Sanjay I. Bidichandani, Tetsuo Ashizawa, and Pragna I. Patel

122 **Linkage Analysis of X-linked Cone-Rod Dystrophy: Localization to Xp11.4 and Definition of a Locus Distinct from RP2 and RP3**
Albert B. Seymour, Anita Dash-Modi, Jeffrey R. O'Connell, Maria Shaffer-Gordon, Tammy S. Mah, S. Tonya Stefko, Ramaiah Nagaraja, Jeremiah Brown, Alan E. Kimura, Robert E. Ferrell, and Michael B. Gorin

130 **Syndromic Ectrodactyly with Severe Limb, Ectodermal, Urogenital, and Palatal Defects Maps to Chromosome 19**
Janis R. O'Quinn, Raoul C. M. Hennekam, Lynn B. Jorde, and Michael Bamshad

136 **The Gene for Severe Combined Immunodeficiency Disease in Athabascan-Speaking Native Americans Is Located on Chromosome 10p**
Lanying Li, Dennis Drayna, Diana Hu, Anthony Hayward, Shiela Gahagan, Henry Pabst, and Morton J. Cowan

145 **Determining Carrier Probabilities for Breast Cancer–Susceptibility Genes BRCA1 and BRCA2**
Giovanni Parmigiani, Donald A. Berry, and Omar Aguilar

159 **Linkage Disequilibrium and Gene Mapping: An Empirical Least-Squares Approach**
Laura C. Lazzeroni

171 **Incorporating Genotypes of Relatives into a Test of Linkage Disequilibrium**
Laurent Excoffier and Montgomery Slatkin

181 **A Test Statistic to Detect Errors in Sib-Pair Relationships**
Margaret Gelder Ehm and Michael Wagner

Letters to the Editor

189 **A De Novo Mutation (Gln2Stop) at the 5′ End of the SRY Gene Leads to Sex Reversal with Partial Ovarian Function**
Stephen Brown, C. C. Yu, Patricia Lanzano, Debra Heller, L. Thomas, Dorothy Warburton, Jan Kitajewski, and Laurel Stadtmauer

192 **Founder Effect, Seen in the British Population, of the 172 Peripherin/*RDS* Mutation—and Further Refinement of Genetic Positioning of the Peripherin/*RDS* Gene**
Annette M. Payne, Susan M. Downes, David A. R. Bessant, Alan C. Bird, and Shomi S. Bhattacharya

195 **Cystic Fibrosis Transmembrane-Conductance Regulator Mutations among African Americans**
K. J. Friedman, M. W. Leigh, P. Czarnecki, and G. L. Feldman

196 **mtDNA Mutations That Cause Optic Neuropathy: How Do We Know?**
Neil Howell, Christy Bogolin, Robyn Jamieson, Daniel R. Marenda, and David A. Mackey

202 **Power, Mode of Inheritance, and Type I Error in Lod Scores and Affecteds-Only Methods: Reply to Kruglyak**
David A. Greenberg, Susan E. Hodge, Veronica J. Vieland, and M. Anne Spence

204 **Efficient Strategies for Genome Scanning with Affected Sib Pairs**
David Curtis

205 **Reply to Curtis**
Peter Holmans and Nick Craddock

Book Review

208 ***The Shape of Life: Genes, Development, and the Evolution of Animal Form.* By Rudolf A. Raff. Chicago and London: The University of Chicago Press, 1996. Pp. 520. $29.95.**
Walter Cressler

Announcements

209 **Employment Opportunities; Meetings; Course**

February 1998

i **This Month in the *Journal***
John Ashkenas

Ecogenetics '98

211 **Comparative Genetics of Resistance to Viruses**
David G. Brownstein

215 **Variability in Immune Response to Pathogens: Using Measles Vaccine to Probe Immunogenetic Determinants of Response**
Gregory A. Poland

Invited Editorial

221 Instant Recognition: The Genetics of Pitch Perception
Peter K. Gregersen

Original Articles

224 Absolute Pitch: An Approach for Identification of Genetic and Nongenetic Components
Siamak Baharloo, Paul A. Johnston, Susan K. Service, Jane Gitschier, and and Nelson B. Freimer

232 Characterization of Mutations in Patients with Multiple Endocrine Neoplasia Type 1
J. H. D. Bassett, S. A. Forbes, A. A. J. Pannett, S. E. Lloyd, P. T. Christie, C. Wooding, B. Harding, G. M. Besser, C. R. Edwards, J. P. Monson, J. Sampson, J. A. H. Wass, M. H. Wheeler, and R. V. Thakker

245 The Haptoglobin-Gene Deletion Responsible for Anhaptoglobinemia
Yoshiro Koda, Mikiko Soejima, Naofumi Yoshioka, and Hiroshi Kimura

253 Topoisomerase I and II Consensus Sequences in a 17-kb Deletion Junction of the *COL4A5* and *COL4A6* Genes and Immunohistochemical Analysis of Esophageal Leiomyomatosis Associated with Alport Syndrome
Yasuyoshi Ueki, Ichiro Naito, Toshitaka Oohashi, Manabu Sugimoto, Tsugio Seki, Hidekatsu Yoshioka, Yoshikazu Sado, Hiroshi Sato, Takashi Sawai, Fumiaki Sasaki, Mitsumasa Matsuoka, Seiji Fukuda, and Yoshifumi Ninomiya

262 Demonstration of a New Pathogenic Mutation in Human Complex I Deficiency: A 5-bp Duplication in the Nuclear Gene Encoding the 18-kD (AQDQ) Subunit
Lambert van den Heuvel, Wim Ruitenbeek, Roel Smeets, Zully Gelman-Kohan, Orly Elpeleg, Jan Loeffen, Frans Trijbels, Edwin Mariman, Diederik de Bruijn, and Jan Smeitink

269 Nearby Stop Codons in Exons of the Neurofibromatosis Type 1 Gene Are Disparate Splice Effectors
Sven Hoffmeyer, Peter Nürnberg, Heide Ritter, Raimund Fahsold, Werner Leistner, Dieter Kaufmann, and Winfrid Krone

278 The DMPK Gene of Severely Affected Myotonic Dystrophy Patients Is Hypermethylated Proximal to the Largely Expanded CTG Repeat
Peter Steinbach, Dieter Gläser, Walther Vogel, Michael Wolf, and Sabine Schwemmle

286 Germ-Line Mutational Analysis of the TSC2 Gene in 90 Tuberous-Sclerosis Patients
Kit-Sing Au, Joseph A. Rodriguez, Jennifer L. Finch, Kelly A. Volcik, E. Steve Roach, Mauricio R. Delgado, Estanislado Rodriguez, Jr., and Hope Northrup

295 HMG CoA Lyase Deficiency: Identification of Five Causal Point Mutations in Codons 41 and 42, Including a Frequent Saudi Arabian Mutation, R41Q
Grant A. Mitchell, Pinar T. Ozand, Marie-France Robert, Lyudmila Ashmarina, Jacqueline Roberts, K. Michael Gibson, Ronald J. Wanders, Shupei Wang, Isabelle Chevalier, E. Plöchl, and Henry Miziorko

301 Ataxia with Isolated Vitamin E Deficiency: Heterogeneity of Mutations and Phenotypic Variability in a Large Number of Families
Laurent Cavalier, Karim Ouahchi, Herbert J. Kayden, Stephano Di Donato, Laurence Reutenauer, Jean-Louis Mandel, and Michel Koenig

311 Diverse Mutations in the Gene for Cartilage Oligomeric Matrix Protein in the Pseudoachondroplasia–Multiple Epiphyseal Dysplasia Disease Spectrum
Michael D. Briggs, Geert R. Mortier, William G. Cole, Lily M. King, Steven S. Golik, Jacky Bonaventure, Lieve Nuytinck, Anne De Paepe, Jules G. Leroy, Leslie Biesecker, Mark Lipson, William R. Wilcox, Ralph S. Lachman, David L. Rimoin, Robert G. Knowlton, and Daniel H. Cohn

320 Mutation Hot Spots in 5q31-Linked Corneal Dystrophies
E. Korvatska, F. L. Munier, A. Djemaï, M. X. Wang, B. Frueh, A. G.-Y. Chiou, S. Uffer, E. Ballestrazzi, R. E. Braunstein, R. K. Forster, W. W. Culbertson, H. Boman, L. Zografos, and D. F. Schorderet

325 Mutations in *CYP1B1*, the Gene for Cytochrome P4501B1, Are the Predominant Cause of Primary Congenital Glaucoma in Saudi Arabia
Bassem A. Bejjani, Richard Alan Lewis, Karim F. Tomey, Kent L. Anderson, David K. Dueker, Monzer Jabak, William F. Astle, Brith Otterud, Mark Leppert, and James R. Lupski

334 *ATM* Mutations and Phenotypes in Ataxia-Telangiectasia Families in the British Isles: Expression of Mutant *ATM* and the Risk of Leukemia, Lymphoma, and Breast Cancer
T. Stankovic, A. M. J. Kidd, A. Sutcliffe, G. M. McGuire, P. Robinson, P. Weber, T. Bedenham, A. R. Bradwell, D. F. Easton, G. G. Lennox, N. Haites, P. J. Byrd, and A. M. R. Taylor

346 Mutations in the EXT1 and EXT2 Genes in Hereditary Multiple Exostoses
Wim Wuyts, Wim Van Hul, Kristel De Boulle, Jan Hendrickx, Egbert Bakker, Filip Vanhoenacker, Florindo Mollica, Hermann-Josef Lüdecke, Bekir Sitki Sayli, Ugo E. Pazzaglia, Geert Mortier, Ben Hamel, Ernest U. Conrad, Mark Matsushita, Wendy H. Raskind, and Patrick J. Willems

355 Linkage of Infantile Bartter Syndrome with Sensorineural Deafness to Chromosome 1p
Theresa M. H. Brennan, Daniel Landau, Hana Shalev, Fred Lamb, Brian C. Schutte, Roxanne Y. Walder, Allyn L. Mark, Rivka Carmi, and Val C. Sheffield

362 Assignment of the Locus for PLO-SL, a Frontal-Lobe Dementia with Bone Cysts, to 19q13
Petra Pekkarinen, Iiris Hovatta, Panu Hakola, Osmo Järvi, Marjo Kestilä, Ulla Lenkkeri, Rolf Adolfsson, Gösta Holmgren, Per-Olof Nylander, Lisbeth Tranebjærg, Joseph D. Terwilliger, Jouko Lönnqvist, and Leena Peltonen

373 Susceptibility to Relapsing-Progressive Multiple Sclerosis Is Associated with Inheritance of Genes Linked to the Variable Region of the TcR β Locus: Use of Affected Family-Based Controls
Michael K. Hockertz, Donald W. Paty, and Steven S. Beall

386 A Gene for Universal Congenital Alopecia Maps to Chromosome 8p21-22
Markus M. Nöthen, Sven Cichon, Ina R. Vogt, Susanne Hemmer, Roland Kruse, Michael Knapp, Tobias Höller, Muhammad Faiyaz ul Haque, Sayedul Haque, Peter Propping, Mahmud Ahmad, and Marcella Rietschel

391 Van Buchem Disease (Hyperostosis Corticalis Generalisata) Maps to Chromosome 17q12-q21
Wim Van Hul, Wendy Balemans, Els Van Hul, Frederik G. Dikkers, Henk Obee, Robert J. Stokroos, Peter Hildering, Filip Vanhoenacker, Guy Van Camp, and Patrick J. Willems

400 The Gene for Glycogen-Storage Disease Type 1b Maps to Chromosome 11q23
Borhane Annabi, Hisayuki Hiraiwa, Brian C. Mansfield, Ke-Jian Lei, Tsuneyuki Ubagai, Mihael H. Polymeropoulos, Shimon W. Moses, Ruti Parvari, Eli Hershkovitz, Hanna Mandel, Moshe Fryman, and Janice Yang Chou

406 Candidate-Gene Studies of the Atherogenic Lipoprotein Phenotype: A Sib-Pair Linkage Analysis of DZ Women Twins
Melissa A. Austin, Philippa J. Talmud, Le-Ahn Luong, Lema Haddad, Ian N. M. Day, Beth Newman, Karen L. Edwards, Ronald M. Krauss, and Steve E. Humphries

420 Different Genetic Components in the Ethiopian Population, Identified by mtDNA and Y-Chromosome Polymorphisms
Giuseppe Passarino, Ornella Semino, Lluís Quintana-Murci, Laurent Excoffier, Michael Hammer, and A. Silvana Santachiara-Benerecetti

435 Mitochondrial Control-Region Sequence Variation in Aboriginal Australians
Sheila M. van Holst Pellekaan, Marianne Frommer, John A. Sved, and Barry Boettcher

450 A Sibship Test for Linkage in the Presence of Association: The Sib Transmission/Disequilibrium Test
Richard S. Spielman and Warren J. Ewens

459 Likelihood Analysis of Disequilibrium Mapping, and Related Problems
Bruce Rannala and Montgomery Slatkin

ASHG Statement

474 Professional Disclosure of Familial Genetic Information
The American Society of Human Genetics Social Issues Subcommittee on Familial Disclosure

Letters to the Editor

484 The −75A→C Substitution in the 5′ UTR of the Wilson Disease Gene Is a Sequence Polymorphism in the Mediterranean Population
Georgios Loudianos, Valeria Dessi, Mario Lovicu, Andrea Angius, Antonio Cao, and Mario Pirastu

484 Reply to Loudianos et al.
Manoj S. Nanji and Diane W. Cox

485 Reply to Burghes
Alex E. MacKenzie

486 Reply to Mackenzie
Arthur Burghes

488 Evidence for Paleolithic and Neolithic Gene Flow in Europe
Guido Barbujani, Giorgio Bertorelle, and Lounès Chikhi

491 Reply to Barbujani et al.
Martin Richards and Bryan Sykes

492 Reply to Hofmann et al.
David Mackey, Roelof-Jan Oostra, Thomas Rosenberg, Eeva Nikoskelainen, Joanna Poulton, Tim Barratt, Pieter Bolhuis, Søren Nørby, Marja-Liisa Savontaus, Christopher Chan, and Neil Howell

495 Characterization of 10p Deletions Suggests Two Nonoverlapping Regions Contribute to the DiGeorge Syndrome Phenotype
Shoshanna Gottlieb, Deborah A. Driscoll, Hope H. Punnett, Beatrice Sellinger, Beverly S. Emanuel, and Marcia L. Budarf

Announcement

499 Conference

Errata

500 Hereditary Nonpolyposis Colorectal Cancer Families Not Complying with the Amsterdam Criteria Show Extremely Low Frequency of Mismatch-Repair-Gene Mutations
Wijnen et al. (August 1997 [61:329–335])

501 De Novo Rearrangements Found in 2% of Index Patients with Spinal Muscular Atrophy: Mutational Mechanisms, Parental Origin, Mutation Rate, and Implications for Genetic Counseling
Wirth et al. (November 1997 [61:1102–1111])

March 1998

i **This Month in the *Journal***
John Ashkenas

Human Genetics '98: Apoptosis

503 **Mechanisms of Cell Death in the Inherited Retinal Degenerations**
Gabriel H. Travis

509 ***CAS*, the Human Homologue of the Yeast Chromosome-Segregation Gene *CSE1*, in Proliferation, Apoptosis, and Cancer**
Ulrich Brinkmann

Insights from Model Systems

514 **Molecular Prophets of Death in the Fly**
Antony Rodriguez, Po Chen, and John M. Abrams

Invited Editorial

520 **The Genetics of Cataract: Our Vision Becomes Clearer**
J. Fielding Hejtmancik

Original Articles

526 **A Missense Mutation in the Human Connexin50 Gene (*GJA8*) Underlies Autosomal Dominant "Zonular Pulverulent" Cataract, on Chromosome 1q**
Alan Shiels, Donna Mackay, Alexander Ionides, Vanita Berry, Anthony Moore, and Shomi Bhattacharya

533 **A Human Homologue of the *Drosophila melanogaster diaphanous* Gene Is Disrupted in a Patient with Premature Ovarian Failure: Evidence for Conserved Function in Oogenesis and Implications for Human Sterility**
Silvia Bione, Cinzia Sala, Chiara Manzini, Giulia Arrigo, Orsetta Zuffardi, Sandro Banfi, Giuseppe Borsani, Philippe Jonveaux, Christophe Philippe, Maurizio Zuccotti, Andrea Ballabio, and Daniela Toniolo

542 **Lack of Homozygotes for the Most Frequent Disease Allele in Carbohydrate-Deficient Glycoprotein Syndrome Type 1A**
Gert Matthijs, Els Schollen, Emile Van Schaftingen, Jean-Jacques Cassiman, and Jaak Jaeken

551 **Genotype-Phenotype Relationships in Ataxia-Telangiectasia and Variants**
Shlomit Gilad, Luciana Chessa, Rami Khosravi, Pamela Russell, Yaron Galanty, Maria Piane, Richard A. Gatti, Timothy J. Jorgensen, Yosef Shiloh, and Anat Bar-Shira

562 **Biochemical Characterization of Arylsulfatase E and Functional Analysis of Mutations Found in Patients with X-Linked Chondrodysplasia Punctata**
Aurora Daniele, Giancarlo Parenti, Marilena d'Addio, Generoso Andria, Andrea Ballabio, and Germana Meroni

573 **Sequence Analysis and Homology Modeling Suggest That Primary Congenital Glaucoma on 2p21 Results from Mutations Disrupting Either the Hinge Region or the Conserved Core Structures of Cytochrome P4501B1**
Ivaylo Stoilov, A. Nurten Akarsu, Ihuoma Alozie, Anne Child, Magda Barsoum-Homsy, M. Erol Turacli, Meral Or, Richard A. Lewis, Nusret Ozdemir, Glen Brice, S. Gulderen Aktan, Line Chevrette, Miguel Coca-Prados, and Mansoor Sarfarazi[1]

585 Splice-Site Mutations: A Novel Genetic Mechanism of Crigler-Najjar Syndrome Type 1
Shailaja Gantla, Conny T. M. Bakker, Bishram Deocharan, Narsing R. Thummala, Jeffry Zweiner, Maarten Sinaasappel, Jayanta Roy Chowdhury, Piter J. Bosma, and Namita Roy Chowdhury

593 Mutation Analysis of Patients with Hermansky-Pudlak Syndrome: A Frameshift Hot Spot in the *HPS* Gene and Apparent Locus Heterogeneity
Jangsuk Oh, Lingling Ho, Sirpa Ala-Mello, Dominick Amato, Linda Armstrong, Sylvia Bellucci, Gerson Carakushansky, Julia P. Ellis, Chin-To Fong, Jane S. Green, Elise Heon, Eric Legius, Alex V. Levin, H. Karel Nieuwenhuis, A. Pinckers, Naoaki Tamura, Margo L. Whiteford, Hisato Yamasaki, and Richard A. Spritz

599 Identification of Novel Mutations in the Ryanodine-Receptor Gene (RYR1) in Malignant Hyperthermia: Genotype-Phenotype Correlation
Bernadette M. Manning, Kathleen A. Quane, Helle Ording, Albert Urwyler, Vincenzo Tegazzin, Mary Lehane, John O'Halloran, Edmund Hartung, Linda M. Giblin, Patrick J. Lynch, Pat Vaughan, Kathrin Censier, Diana Bendixen, Giacomo Comi, Luc Heytens, Koen Monsieurs, Tore Fagerlund, Werner Wolz, James J. A. Heffron, Clemens R. Muller, and Tommie V. McCarthy

610 Frequency of Somatic and Germ-Line Mosaicism in Retinoblastoma: Implications for Genetic Counseling
Kimberly C. Sippel, Rebecca E. Fraioli, Gary D. Smith, Mary E. Schalkoff, Joanne Sutherland, Brenda L. Gallie, and Thaddeus P. Dryja

620 Assignment of the Tibial Muscular Dystrophy Locus to Chromosome 2q31
Henna Haravuori, Päivi Mäkelä-Bengs, Bjarne Udd, Juhani Partanen, Leena Pulkkinen, Hannu Somer, and Leena Peltonen

627 Mapping of X-Linked Myxomatous Valvular Dystrophy to Chromosome Xq28
Florence Kyndt, Jean-Jacques Schott, Jean-Noël Trochu, Florence Baranger, Odile Herbert, Valérie Scott, Edith Fressinaud, Albert David, Jean-Paul Moisan, Jean-Brieuc Bouhour, Hervé Le Marec, and Bernard Bénichou

633 Linkage of the Gene for an Autosomal Dominant Form of Juvenile Amyotrophic Lateral Sclerosis to Chromosome 9q34
Phillip F. Chance, Bruce A. Rabin, Stephen G. Ryan, Yuan Ding, Mena Scavina, Barbara Crain, John W. Griffin, and David R. Cornblath

641 Localization of the Fourth Locus (GLC1E) For Adult-Onset Primary Open-Angle Glaucoma to the 10p15-p14 Region
Mansoor Sarfarazi, Anne Child, Diliana Stoilova, Glen Brice, Trushna Desai, Ovidiu C. Trifan, Darmalingum Poinoosawmy, and R. Pitts Crick

653 Linkage Analysis of Chromosome 1q Markers in 136 Prostate Cancer Families
Rosalind A. Eeles, Francine Durocher, Steve Edwards, Dawn Teare, Mike Badzioch, Rifat Hamoudi, Sandra Gill, Patrick Biggs, David Dearnaley, Audrey Ardern-Jones, Anna Dowe, Robert Shearer, Dawn L. McLennan, Richard L. Norman, Parviz Ghadirian, Armen Aprikian, Deborah Ford, Chris Amos, Terri M. King, The Cancer Research Campaign/British Prostate Group U.K. Familial Prostate Cancer Study Collaborators, Fernand Labrie, Jacques Simard, Steven A. Narod, Douglas Easton, and William D. Foulkes

659 Autosomal Genomic Scan for Loci Linked to Obesity and Energy Metabolism in Pima Indians
R. A. Norman, P. A. Tataranni, R. Pratley, D. B. Thompson, R. L. Hanson, M. Prochazka, L. Baier, M. G. Ehm, H. Sakul, T. Foroud, W. T. Garvey, D. Burns, W. C. Knowler, P. H. Bennett, C. Bogardus, and E. Ravussin

669 Genome Search in Celiac Disease
Luigi Greco, Gino Corazza, Marie-Claude Babron, Fabienne Clot, Marie-Claude Fulchignoni-Lataud, Selvaggia Percopo, Patrizia Zavattari, Faouzi Bouguerra, Colette Dib, Roberto Tosi, Riccardo Troncone, Alessandro Ventura, Wilma Mantavoni, Giuseppe Magazzù, Rosanna Gatti, Rosanna Lazzari, Annamaria Giunta, Francesco Perri, Giuseppe Iacono, Ettore Cardi, Stefano de Virgiliis, Francesco Cataldo, Gianluigi De Angelis, Salvatore Musumeci, Roberto Ferrari, Fiorella Balli, Maria-Teresa Bardella, Umberto Volta, Carlo Catassi, Giuliano Torre, Jean-François Eliaou, Jean-Louis Serre, and Françoise Clerget-Darpoux

676 Genetic Heterogeneity and Penetrance Analysis of the BRCA1 and BRCA2 Genes in Breast Cancer Families
D. Ford, D. F. Easton, M. Stratton, S. Narod, D. Goldgar, P. Devilee, D. T. Bishop, B. Weber, G. Lenoir, J. Chang-Claude, H. Sobol, M. D. Teare, J. Struewing, A. Arason, S. Scherneck, J. Peto, T. R. Rebbeck, P. Tonin, S. Neuhausen, R. Barkardottir, J. Eyfjord, H. Lynch, B. A. J. Ponder, S. A. Gayther, J. M. Birch, A. Lindblom, D. Stoppa-Lyonnet, Y. Bignon, A. Borg, U. Hamann, N. Haites, R. J. Scott, C. M. Maugard, H. Vasen, S. Seitz, L. A. Cannon-Albright, A. Schofield, M. Zelada-Hedman, and Breast Cancer Linkage Consortium

690 Significance Levels in Complex Inheritance
Newton E. Morton

698 On the Probabilities of Identity States in Permutable Populations
C. Cannings

703 Marker Selection for the Transmission/Disequilibrium Test, in Recently Admixed Populations
N. L. Kaplan, E. R. Martin, R. W. Morris, and B. S. Weir

Letters to the Editor

713 A *BRCA1* Nonsense Mutation Causes Exon Skipping
Sylvie Mazoyer, Nadine Puget, Laure Perrin-Vidoz, Henry T. Lynch, Olga M. Serova-Sinilnikova, and Gilbert M. Lenoir

715 Mutations of the *RET-GDNF* Signaling Pathway in Ondine's Curse
Jeanne Amiel, Rémi Salomon, Tania Attié, Anna Pelet, Ha Trang, Mustapha Mokhtari, Claude Gaultier, Arnold Munnich, and Stanislas Lyonnet

717 De Novo mtDNA nt 8993 (T→G) Mutation Resulting in Leigh Syndrome
Satoru Takahashi , Yoshio Makita, Junichi Oki, Akie Miyamoto, Junichi Yanagawa, Etsuo Naito, Yu-ichi Goto, and Akimasa Okuno

719 A Kerato-Epithelin (βig-h3) Mutation in Lattice Corneal Dystrophy Type IIIA
Shuji Yamamoto, Masaki Okada, Motokazu Tsujikawa, Yoshikazu Shimomura, Kohji Nishida, Yoshitsugu Inoue, Hitoshi Watanabe, Naoyuki Maeda, Hiroki Kurahashi, Shigeru Kinoshita, Yusuke Nakamura, and Yasuo Tano

723 A Causative Relationship between Mutant *IFNgR1* Alleles and Impaired Cellular Response to IFNγ in a Compound Heterozygous Child
Frédéric Altare, Emmanuelle Jouanguy, Salma Lamhamedi-Cherradi, Marie-Claude Fondanèche, Cécile Fizame, Florence Ribiérre, Gilles Merlin, Zlatko Dembic, Robert Schreiber, Barbara Lisowska-Grospierre, Alain Fischer, Eric Seboun, and Jean-Laurent Casanova

726 On the Probability of Identity States in Permutable Populations: Reply to Cannings
Emmanuelle Génin, Hadi Quesneville, and Françoise Clerget-Darpoux

728 Consanguinity and Relative-Pair Methods for Linkage Analysis
Daniel E. Weeks and Janet S. Sinsheimer

731 Reply to Weeks and Sinsheimer
Emmanuelle Génin and Françoise Clerget-Darpoux

736 Health, Life, and Disability Insurance and Hereditary Nonpolyposis Colorectal Cancer
Miguel A. Rodriguez-Bigas, Hans F. A. Vasen, Linda O'Malley, Mary-Jo T. Rosenblatt, Carolyn Farrell, Thomas K. Weber, and Nicholas J. Petrelli

738 Likelihood Calculation Conditional on Observed Pedigree Structure
P. Mahinda Karunaratne and Robert C. Elston

739 **Reply to Karunaratne and Elston**
Veronica J. Vieland and Susan E. Hodge

Announcements

741 **Employment Opportunities; Meetings; Workshops; Course; Genetic Counseling Certification; Immunogenetics Database; Mutation Panel**

April 1998

i **This Month in the *Journal***
John Ashkenas

Mitochondrial Genetics '98

745 **The Myoclonic Epilepsy and Ragged-Red Fiber Mutation Provides New Insights into Human Mitochondrial Function and Genetics**
Anne Chomyn

752 **Is the Bottleneck Cracked?**
J. Poulton, V. Macaulay, and D. R. Marchington

758 **Mitochondrial Dysfunction in Idiopathic Parkinson Disease**
W. Davis Parker, Jr. and Russell H. Swerdlow

Invited Editorials

763 **Fetal DNA in Maternal Plasma: The Plot Thickens and the Placental Barrier Thins**
Diana W. Bianchi

765 **Are We Ready to Try to Cure Alkaptonuria?**
Bert N. La Du, Jr.

Original Articles

768 **Quantitative Analysis of Fetal DNA in Maternal Plasma and Serum: Implications for Noninvasive Prenatal Diagnosis**
Y. M. Dennis Lo, Mark S. C. Tein, Tze K. Lau, Christopher J. Haines, Tse N. Leung, Priscilla M. K. Poon, James S. Wainscoat, Philip J. Johnson, Allan M. Z. Chang, and N. Magnus Hjelm

776 **Mutation and Polymorphism Analysis of the Human Homogentisate 1,2-Dioxygenase Gene in Alkaptonuria Patients**
D. Beltrán-Valero de Bernabé, B. Granadino, I. Chiarelli, B. Porfirio, E. Mayatepek, R. Aquaron, M. M. Moore, J. J. M. Festen, R. Sanmartí, M. A. Peñalva, and S. Rodríguez de Córdoba

785 **Mutations in the Liver Glycogen Phosphorylase Gene (*PYGL*) Underlying Glycogenosis Type VI (Hers Disease)**
Barbara Burwinkel, Henk D. Bakker, Eliezer Herschkovitz, Shimon W. Moses, Yoon S. Shin, and Manfred W. Kilimann

792 Novel Mutations in the Connexin 26 Gene (GJB2) That Cause Autosomal Recessive (DFNB1) Hearing Loss
P. M. Kelley, D. J. Harris, B. C. Comer, J. W. Askew, T. Fowler, S. D. Smith, and W. J. Kimberling

800 *OA1* Mutations and Deletions in X-Linked Ocular Albinism
Rhonda E. Schnur, Mei Gao, Penelope A. Wick, Margaret Keller, Paul J. Benke, Matthew J. Edwards, Arthur W. Grix, Athel Hockey, Jack H. Jung, Kenneth K. Kidd, Mildred Kistenmacher, Alex V. Levin, Richard A. Lewis, Maria A. Musarella, Rod W. Nowakowski, Seth J. Orlow, Roberta S. Pagon, De-Ann M. Pillers, Hope H. Punnett, Graham E. Quinn, Kamer Tezcan, Joseph Wagstaff, and Richard G. Weleber

810 Evidence That Lymphangiomyomatosis Is Caused by *TSC2* Mutations: Chromosome 16p13 Loss of Heterozygosity in Angiomyolipomas and Lymph Nodes from Women with Lymphangiomyomatosis
Teresa A. Smolarek, Lisa L. Wessner, Francis X. McCormack, Johanna C. Mylet, Anil G. Menon, and Elizabeth Petri Henske

816 Marshall Syndrome Associated with a Splicing Defect at the *COL11A1* Locus
Andrew J. Griffith, Leslie K. Sprunger, D. Alexa Sirko-Osadsa, George E. Tiller, Miriam H. Meisler, and Matthew L. Warman

824 Identification of Constitutional WT1 Mutations, in Patients with Isolated Diffuse Mesangial Sclerosis, and Analysis of Genotype/Phenotype Correlations by Use of a Computerized Mutation Database
C. Jeanpierre, E. Denamur, I. Henry, M.-O. Cabanis, S. Luce, A. Cécille, J. Elion, M. Peuchmaur, C. Loirat, P. Niaudet, M.-C. Gubler, and C. Junien

834 A Clinical Variant of Neurofibromatosis Type 1: Familial Spinal Neurofibromatosis with a Frameshift Mutation in the *NF1* Gene
Elisabet Ars, Helena Kruyer, Antonia Gaona, Pilar Casquero, Jordi Rosell, Víctor Volpini, Eduard Serra, Conxi Lázaro, and Xavier Estivill

842 A PCR Amplification Method Reveals Instability of the Dodecamer Repeat in Progressive Myoclonus Epilepsy (EPM1) and No Correlation between the Size of the Repeat and Age at Onset
Maria D. Lalioti, Hamish S. Scott, Pierre Genton, Djamel Grid, Réda Ouazzani, Amel M'Rabet, Sadi Ibrahim, Riadh Gouider, Charlotte Dravet, Taieb Chkili, Armand Bottani, Catherine Buresi, Alain Malafosse, and Stylianos E. Antonarakis

848 Paternal Uniparental Disomy for Chromosome 1 Revealed by Molecular Analysis of a Patient with Pycnodysostosis
Bruce D. Gelb, Judith P. Willner, Teresa M. Dunn, Nataline B. Kardon, Alain Verloes, Jacques Poncin, and Robert J. Desnick

855 DAX1 Mutations Map to Putative Structural Domains in a Deduced Three-Dimensional Model
Yao-Hua Zhang, Weiwen Guo, Richard L. Wagner, Bing-Ling Huang, Linda McCabe, Eric Vilain, Thomas P. Burris, Kwame Anyane-Yeboa, Arthur H. M. Burghes, David Chitayat, Albert E. Chudley, Myron Genel, Joseph M. Gertner, Georgeanna J. Klingensmith, Steven N. Levine, Jon Nakamoto, Maria I. New, Roberta A. Pagon, John G. Pappas, Charmian A. Quigley, Ira M. Rosenthal, John D. Baxter, Robert J. Fletterick, and Edward R. B. McCabe

865 Evidence for Genetic Heterogeneity in X-Linked Congenital Stationary Night Blindness
Kym M. Boycott, William G. Pearce, Maria A. Musarella, Richard G. Weleber, Tracy A. Maybaum, David G. Birch, Yozo Miyake, Rockefeller S. L. Young, and N. Torben Bech-Hansen

876 Genetic Linkage of Hereditary Gingival Fibromatosis to Chromosome 2p21
Thomas C. Hart, Debora Pallos, Donald W. Bowden, Joey Bolyard, Mark J. Pettenati, and Jose R. Cortelli

884 Gene Localization for an Autosomal Dominant Familial Periodic Fever to 12p13
John Mulley, Kathrin Saar, Gerry Hewitt, Franz Rüschendorf, Hilary Phillips, Alison Colley, David Sillence, André Reis, and Meredith Wilson

890 Refined Genetic Mapping of the Darier Locus to a <1-cM Region of Chromosome 12q24.1, and Construction of a Complete, High-Resolution P1 Artificial Chromosome/Bacterial Artificial Chromosome Contig of the Critical Region
Sarah Monk, Anavaj Sakuntabhai, Simon A. Carter, Steven D. Bryce, Roger Cox, Louise Harrington, Elaine Levy, Victor L. Ruiz-Perez, Eleni Katsantoni, Ahmer Kodvawala, Colin S. Munro, Susan Burge, Marc Larrègue, Gyula Nagy, Jonathan L. Rees, Mark Lathrop, Anthony P. Monaco, Tom Strachan, and Alain Hovnanian

904 Genetic Mapping Refines *DFNB3* to 17p11.2, Suggests Multiple Alleles of *DFNB3,* and Supports Homology to the Mouse Model *shaker-2*
Yong Liang, Aihui Wang, Frank J. Probst, I. Nyoman Arhya, Thomas D. Barber, Ken-Shiung Chen, Dilip Deshmukh, David F. Dolan, John T. Hinnant, Lynn E. Carter, Pawan K. Jain, Anil K. Lalwani, Xiaoyan C. Li, James R. Lupski, Sukarti Moeljopawiro, Robert Morell, Clelia Negrini, Edward R. Wilcox, Sunaryana Winata, Sally A. Camper, and Thomas B. Friedman

916 No Evidence for Significant Linkage between Bipolar Affective Disorder and Chromosome 18 Pericentromeric Markers in a Large Series of Multiplex Extended Pedigrees
James A. Knowles, Peter A. Rao, Tara Cox-Matise, Jo Ellen Loth, Graciel!e M. de Jesus, Laura Levine, Kamna Das, Graciela K. Penchaszadeh, Joyce R. Alexander, Bernard Lerer, Jean Endicott, Jurg Ott, T. Conrad Gilliam, and Miron Baron

925 Molecular Cytogenetic Evidence for a Common Breakpoint in the Largest Inverted Duplications of Chromosome 15
A. E. Wandstrat, J. Leana-Cox, L. Jenkins, and S. Schwartz

937 Polymorphic Detection of a Parthenogenetic Maternal and Double Paternal Contribution to a 46,XX/46,XY Hermaphrodite
Jacques C. Giltay, Tibor Brunt, Frits A. Beemer, Jan-Maarten Wit, Hans Kristian Ploos van Amstel, Peter L. Pearson, and Cisca Wijmenga

941 Using Neural Networks as an Aid in the Determination of Disease Status: Comparison of Clinical Diagnosis to Neural-Network Predictions in a Pedigree with Autosomal Dominant Limb-Girdle Muscular Dystrophy
Catherine T. Falk, James M. Gilchrist, Margaret A. Pericak-Vance, and Marcy C. Speer

950 Genetic Association Mapping Based on Discordant Sib Pairs: The Discordant-Alleles Test
Michael Boehnke and Carl D. Langefeld

962 The Quantitative LOD Score: Test Statistic and Sample Size for Exclusion and Linkage of Quantitative Traits in Human Sibships
Grier P. Page, Christopher I. Amos, and Eric Boerwinkle

969 A Log-Linear Approach to Case-Parent–Triad Data: Assessing Effects of Disease Genes That Act Either Directly or through Maternal Effects and That May Be Subject to Parental Imprinting
C. R. Weinberg, A. J. Wilcox, and R. T. Lie

979 Determinism and Mass-Media Portrayals of Genetics
Celeste M. Condit, Nneka Ofulue, and Kristine M. Sheedy

Letters to the Editor

985 HLA and Mate Choice
Thomas J. Gill

986 Reply to Gill
Lowell R. Weitkamp and Carole Ober

987 A Locus for Autosomal Recessive Hypodontia with Associated Dental Anomalies Maps to Chromosome 16q12.1
Wasim Ahmad, Valeria Brancolini, Muhammad Faiyaz ul Haque, HaMut Lam, Sayed ul Haque, Mahmud Haider, Aijaz Maimon, Vincent M. Aita, Jason Owen, Donna Brown, David J. Zegarelli, Mahmud Ahmad, Jurg Ott, and Angela M. Christiano

991 The African Origin of the Common Mutation in African American Patients with Glycogen-Storage Disease Type II
Jeffrey A. Becker, John Vlach, Nina Raben, Kanneboyina Nagaraju, Elizabeth M. Adams, Monique M. Hermans, Arnold J. J. Reuser, Susan Sklower Brooks, Cynthia J. Tifft, Rochelle Hirschhorn, Maryann L. Huie, Marc Nicolino, and Paul H. Plotz

994 Linkage Thresholds for Two-stage Genome Scans
Leonid Kruglyak and Mark J. Daly

996 Response to Kruglyak
Stephen Sawcer, Hywel B. Jones, and David Clayton

Book Reviews

998 *Genetic Skin Disorders.* By Virginia P. Sybert
John C. Carey

999 *Handbook of Psychiatric Genetics.* Edited by Kenneth Blum and Ernest P. Noble
Nick Craddock

Announcements

1000 Employment and Fellowship Opportunities; Training Program; Call for Patients; Call for Nominations; Regional Mapping Panels; Summer School; Human Diversity Panels

May 1998

i This Month in the *Journal*
John Ashkenas

Human Genetics '98

1003 Replicative Senescence in the Immune System: Impact of the Hayflick Limit on T-Cell Function in the Elderly
Rita B. Effros

1008 Causes, Effects, and Constraints in the Genetics of Human Longevity
François Schächter

Insights from Model Systems

1015 The Genetics of Cellular Senescence
Nathalie G. Bérubé, James R. Smith, and Olivia M. Pereira-Smith

Invited Editorial

1020 Molecular Classification of the Inherited Hamartoma Polyposis Syndromes: Clearing the Muddied Waters
Charis Eng and HanLee Ji

Original Articles

1023 Human Meiotic Recombination Products Revealed by Sequencing a Hotspot for Homologous Strand Exchange in Multiple HNPP Deletion Patients
Lawrence T. Reiter, Philip J. Hastings, Eva Nelis, Peter De Jonghe, Christine Van Broeckhoven, and James R. Lupski

1034 Mutations in Btk in Patients with Presumed X-Linked Agammaglobulinemia
Mary Ellen Conley, Derrick Mathias, Jason Treadaway, Yoshiyuki Minegishi, and Jurg Rohrer

1044 A Second Common Mutation in the Methylenetetrahydrofolate Reductase Gene: An Additional Risk Factor for Neural-Tube Defects?
Nathalie M. J. van der Put, Fons Gabreëls, Erik M. B. Stevens, Jan A. M. Smeitink, Frans J. M. Trijbels, Tom K. A. B. Eskes, Lambert P. van den Heuvel, and Henk J. Blom

1052 Genotype/Phenotype Correlation in Autosomal Recessive Lamellar Ichthyosis
Hans Christian Hennies, Wolfgang Küster, Victor Wiebe, Alice Krebsová, and André Reis

1062 Localization of the Gene for Congenital Dyserythropoietic Anemia Type I to a <1-cM Interval on Chromosome 15q15.1-15.3
Hannah Tamary, Lea Shalmon, Hanna Shalev, Albudar Halil, Dina Dobrushin, Noga Ashkenazi, Meira Zoldan, Peretz Resnitzky, Michael Korostishevsky, Batsheva Bonne-Tamir, and Rina Zaizov

1070 A Syndrome of Severe Mental Retardation, Spasticity, and Tapetoretinal Degeneration Linked to Chromosome 15q24
S. J. Mitchell, D. P. McHale, D. A. Campbell, N. J. Lench, R. F. Mueller, S. E. Bundey, and A. F. Markham

1077 Linkage-Disequilibrium Mapping of Autistic Disorder, with 15q11-13 Markers
Edwin H. Cook, Rachel Y. Courchesne, Nancy J. Cox, Catherine Lord, David Gonen, Stephen J. Guter, Alan Lincoln, Kristi Nix, Richard Haas, Bennett L. Leventhal, and Eric Courchesne

1084 A Susceptibility Locus for Bipolar Affective Disorder on Chromosome 4q35
Linda J. Adams, Philip B. Mitchell, Sharon L. Fielder, Amanda Rosso, Jennifer A. Donald, and Peter R. Schofield

1092 Renpenning Syndrome Maps to Xp11
Roger E. Stevenson, J. Fernando Arena, Elizabeth Ouzts, Alice Gibson, M. H. K. Shokeir, Cindy Vnencak-Jones, Herbert A. Lubs, M. May, and Charles E. Schwartz

1102 A Gene for Autosomal Dominant Hypohidrotic Ectodermal Dysplasia (*EDA3*) Maps to Chromosome 2q11-q13
Lingling Ho, Marc S. Williams, and Richard A. Spritz

1107 The Bjornstad Syndrome (Sensorineural Hearing Loss and Pili Torti) Disease Gene Maps to Chromosome 2q34-36
José Faibes Lubianca Neto, Leonard Lu, Roland D. Eavey, Marco Antonio Macias Flores, Raul Martinez Caldera, Somkiat Sangwatanaroj, Jean Jacques Schott, Barbara McDonough, Jose Ignatio Santos, Christine E. Seidman, and J. G. Seidman

1113 A Locus for Autosomal Recessive Congenital Microphthalmia Maps to Chromosome 14q32
David A. R. Bessant, Shagufta Khaliq, Abdul Hameed, Khalid Anwar, S. Qasim Mehdi, Annette M. Payne, and Shomi S. Bhattacharya

1117 **Mapping of a Congenital Microcoria Locus to 13q31-q32**
Christelle Rouillac, Olivier Roche, Dominique Marchant, Lucien Bachner, Alexandra Kobetz, Pierre-Jean Toulemont, Christophe Orssaud, Martine Urvoy, Sylvie Odent, Bernard Le Marec, Marc Abitbol, and Jean-Louis Dufier

1123 **Autozygosity Mapping, to Chromosome 11q25, of a Rare Autosomal Recessive Syndrome Causing Histiocytosis, Joint Contractures, and Sensorineural Deafness**
Leanne M. Moynihan, Sarah E. Bundey, David Heath, E. Lynn Jones, Duncan P. McHale, Robert F. Mueller, Alexander F. Markham, and Nicholas J. Lench

1129 **A Gene for Familial Juvenile Polyposis Maps to Chromosome 18q21.1**
James R. Howe, John C. Ringold, Robert W. Summers, Frank A. Mitros, D. Y. Nishimura, and Edwin M. Stone

1137 **mtDNA Analysis Reveals a Major Late Paleolithic Population Expansion from Southwestern to Northeastern Europe**
Antonio Torroni, Hans-Jürgen Bandelt, Leila D'Urbano, Päivi Lahermo, Pedro Moral, Daniele Sellitto, Chiara Rengo, Peter Forster, Marja-Liisa Savontaus, Batsheva Bonné-Tamir, and Rosaria Scozzari

1153 **mtDNA Analysis of a Prehistoric Oneota Population: Implications for the Peopling of the New World**
Anne C. Stone and Mark Stoneking

1171 **Dual Origins of Finns Revealed by Y Chromosome Haplotype Variation**
Rick A. Kittles, Markus Perola, Leena Peltonen, Andrew W. Bergen, Richard A. Aragon, Matti Virkkunen, Markku Linnoila, David Goldman, and Jeffrey C. Long

1180 **An Analysis of Linkage Disequilibrium in the Interleukin-1 Gene Cluster, Using a Novel Grouping Method for Multiallelic Markers**
Angela Cox, Nicola J. Camp, Martin J. H. Nicklin, Francesco S. di Giovine, and Gordon W. Duff

1189 **A Simple Method for Analyzing Microsatellite Allele Image Patterns Generated from DNA Pools and Its Application to Allelic Association Studies**
Johanna Daniels, Peter Holmans, Nigel Williams, Dragana Turic, Peter McGuffin, Robert Plomin, and Michael J. Owen

1198 **Multipoint Quantitative-Trait Linkage Analysis in General Pedigrees**
Laura Almasy and John Blangero

1212 **Statistical Evaluation of Age-at-Onset Anticipation: A New Test and Evaluation of Its Behavior in Realistic Applications**
Veronica J. Vieland and Jian Huang

1228 **Simple, Robust Linkage Tests for Affected Sibs**
Alice S. Whittemore and I-Ping Tu

ACMG/ASHG Statement

1243 **Laboratory Guidelines for Huntington Disease Genetic Testing**
The American College of Medical Genetics/American Society of Human Genetics Huntington Disease Genetic Testing Working Group

Letters to the Editor

1248 **Segregation of a *PRKCG* Mutation in Two RP11 Families**
Mai Al-Maghtheh, Eranga N. Vithana, Chris F. Inglehearn, Tony Moore, Alan C. Bird, and Shomi S. Bhattacharya

1252 **Diversity of Cystic Fibrosis Mutation-Screening Practices**
Wayne W. Grody, Robert J. Desnick, Nancy J. Carpenter, and Walter W. Noll

1254 Linkage Disequilibrium Analysis in a Recently Founded Population: Evaluation of the Variegate Porphyria Founder in South African Afrikaners
Johannes Z. Groenewald, Junita Liebenberg, Ilse M. Groenewald, and Louise Warnich

1258 Worldwide Distribution of a Common Methylenetetrahydrofolate Reductase Mutation
Julie A. Schneider, David C. Rees, Yan-Tat Liu, and John B. Clegg

1260 Mutational Mechanisms for Generating Microsatellite Allele-Frequency Distributions: An Analysis of 4,558 Markers
Martin Farrall and Daniel E. Weeks

1262 Some Underlooked Properties of the Multifactorial/Threshold Model
F. Clarke Fraser

Announcements

1266 Conference; Cell Cultures

Errata

1267 Human Genetic Affinities for Y-Chromosome P49a,f/*Taq*I Haplotypes Show Strong Correspondence with Linguistics
Poloni et al. (November 1997 [61:1015–1035])

1267 Susceptibility to Relapsing-Progressive Multiple Sclerosis Is Associated with Inheritance of Genes Linked to the Variable Region of the TcR β Locus: Use of Affected Family-Based Controls
Hockertz et al. (February 1998 [62:373–385])

June 1998

i This Month in the *Journal*
John Ashkenas

Gametogenesis '98

1269 Cytosine Methylation and the Unequal Developmental Potentials of the Oocyte and Sperm Genomes
Timothy H. Bestor

1274 Male Infertility and the Genetics of Spermatogenesis
Masaru Okabe, Masahito Ikawa, and John Ashkenas

Insights from Model Systems

1282 Genetic Causes of Female Infertility: Targeted Mutagenesis in Mice
Stephen Greenhouse, Tracy Rankin, and Jurrien Dean

1285 Technical Sidebar: "Humanizing" the Mouse Egg Coat

Invited Editorial

1288 Classification of Familial Adenomatous Polyposis: A Diagnostic Nightmare
Henry T. Lynch and Thomas C. Smyrk

Original Articles

1290 Genotype-Phenotype Correlations in Attenuated Adenomatous Polyposis Coli
Claudio Soravia, Terri Berk, Lisa Madlensky, Angela Mitri, Hong Cheng, Steven Gallinger, Zane Cohen, and Bharati Bapat

1302 Hyperphenylalaninemia with High Levels of 7-Biopterin is Associated with Mutations in the *PCBD* Gene Encoding the Bifunctional Protein Pterin-4a-Carbinolamine Dehydratase and Transcriptional Coactivator (DCoH)
Beat Thöny, Frank Neuheiser, Lucja Kierat, Milan Blaskovics, Pamela H. Arn, Patrick Ferreira, Igor Rebrin, June Ayling, and Nenad Blau

1312 Amerindian Pyruvate Carboxylase Deficiency Is Associated with Two Distinct Missense Mutations
Mary Anna Carbone, Nevi MacKay, Mingfu Ling, David E. C. Cole, Cheryl Douglas, Brigitte Rigat, Annette Feigenbaum, Joe T. R. Clarke, James C. Haworth, Cheryl R. Greenberg, Lorne Seargeant, and Brian H. Robinson

1320 X-Linked Chronic Granulomatous Disease: Mutations in the *CYBB* Gene Encoding the gp91-*phox* Component of Respiratory-Burst Oxidase
Julie Rae, Peter E. Newburger, Mary C. Dinauer, Deborah Noack, Penelope J. Hopkins, Ryoko Kuruto, and John T. Curnutte

1332 Novel Molecular Variants of the Na-K-2Cl Cotransporter Gene Are Responsible for Antenatal Bartter Syndrome
Rosa Vargas-Poussou, Delphine Feldmann, Martin Vollmer, Martin Konrad, Lisa Kelly, Lambertus P. W. J. van den Heuvel, Lamia Tebourbi, Matthias Brandis, Lothar Karolyi, Steven C. Hebert, Henny H. Lemmink, Georges Deschênes, Friedhelm Hildebrandt, Hannsjörg W. Seyberth, Lisa M. Guay-Woodford, Nine V. A. M. Knoers, and Corinne Antignac

1341 Systematic Analysis of Molecular Defects in the Ferrochelatase Gene from Patients with Erythropoietic Protoporphyria
U. B. Rüfenacht, L. Gouya, X. Schneider-Yin, H. Puy, B. W. Schäfer, R. Aquaron, Y. Nordmann, E. I. Minder, and J. C. Deybach

1353 Mutation Analysis of UBE3A in Angelman Syndrome Patients
Perrine Malzac, Hayley Webber, Anne Moncla, John M. Graham, Mary Kukolich, Charles Williams, Roberta A. Pagon, Linda A. Ramsdell, Tatsuya Kishino, and Joseph Wagstaff

1361 Spectrum and Frequency of *Jagged1* (*JAG1*) Mutations in Alagille Syndrome Patients and Their Families
Ian D. Krantz, Raymond P. Colliton, Anna Genin, Elizabeth B. Rand, Linheng Li, David A. Piccoli, and Nancy B. Spinner

1370 Genetic Heterogeneity of Saethre-Chotzen Syndrome, Due to *TWIST* and *FGFR* Mutations
William A. Paznekas, Michael L. Cunningham, Timothy D. Howard, Bruce R. Korf, Mark H. Lipson, Art W. Grix, Murray Feingold, Rosalie Goldberg, Zvi Borochowitz, Kirk Aleck, John Mulliken, Mingfei Yin, and Ethylin Wang Jabs

1381 Haplotype and Phenotype Analysis of Nine Recurrent *BRCA2* Mutations in 111 Families: Results of an International Study
Susan L. Neuhausen, Andrew K. Godwin, Ruth Gershoni-Baruch, Elizabeth Schubert, Judy Garber, Dominique Stoppa-Lyonnet, Edith Olah, Bela Csokay, Olga Serova, Fiona Lalloo, Ana Osorio, Michael Stratton, Kenneth Offit, Jeff Boyd, M. Adelaide Caligo, Rodney J. Scott, Andy Schofield, Eric Teugels, Manfred Schwab, Lisa Cannon-Albright, Timothy Bishop, Douglas Easton, Javier Benitez, Mary-Claire King, Bruce A. J. Ponder, Barbara Weber, Peter Devilee, Åke Borg, Steven A. Narod, and David Goldgar

1389 A Global Haplotype Analysis of the Myotonic Dystrophy Locus: Implications for the Evolution of Modern Humans and for the Origin of Myotonic Dystrophy Mutations
S. A. Tishkoff, A. Goldman, F. Calafell, W. C. Speed, A. S. Deinard, B. Bonne-Tamir, J. R. Kidd, A. J. Pakstis, T. Jenkins, and K. K. Kidd

1403 The Hemochromatosis 845 G→A and 187 C→G Mutations: Prevalence in Non-Caucasian Populations
Lara M. Cullen, Xiaojiang Gao, Simon Easteal, and Elizabeth C. Jazwinska

1408 Mutation Rate in Human Microsatellites: Influence of the Structure and Length of the Tandem Repeat
Bernd Brinkmann, Michael Klintschar, Franz Neuhuber, Julia Hühne, and Burkhard Rolf

1416 Predisposing Gene for Early-Onset Prostate Cancer, Localized on Chromosome 1q42.2-43
Philippe Berthon, Antoine Valeri, Annick Cohen-Akenine, Eric Drelon, Thomas Paiss, Gudrun Wöhr, Alain Latil, Philippe Millasseau, Imène Mellah, Nadine Cohen, Hélène Blanché, Christine Bellané-Chantelot, Florence Demenais, Pierre Teillac, Alain Le Duc, Robert de Petriconi, Richard Hautmann, Ilya Chumakov, Lucien Bachner, Norman J. Maitland, Rosette Lidereau, Walther Vogel, Georges Fournier, Philippe Mangin, Daniel Cohen, and Olivier Cussenot

1425 Evidence for Autosomal Dominant Inheritance of Prostate Cancer
Daniel J. Schaid, Shannon K. McDonnell, Michael L. Blute, and Stephen N. Thibodeau

1439 Identification of a New Locus for a Peculiar Form of Congenital Muscular Dystrophy with Early Rigidity of the Spine, on Chromosome 1p35-36
Behzad Moghadaszadeh, Isabelle Desguerre, Haluk Topaloglu, Francesco Muntoni, Sylvana Pavek, Caroline Sewry, Michèle Mayer, Michel Fardeau, Fernando M. S. Tomé, and Pascale Guicheney

1446 Linkage of Familial Hibernian Fever to Chromosome 12p13
Michael F. McDermott, B. William Ogunkolade, Elizabeth M. McDermott, Lisa C. Jones, Ying Wan, Kathleen A. Quane, John McCarthy, Mark Phelan, Michael G. Molloy, Richard J. Powell, Christopher I. Amos, and Graham A. Hitman

1452 A Major Locus for Autosomal Recessive Retinitis Pigmentosa on 6q, Determined by Homozygosity Mapping of Chromosomal Regions That Contain Gamma-Aminobutyric Acid–Receptor Clusters
Agustín Ruiz, Salud Borrego, Irene Marcos, and Guillermo Antiñolo

1460 Genetic Mapping of Ossification of the Posterior Longitudinal Ligament of the Spine
Hiroaki Koga, Takashi Sakou, Eiji Taketomi, Kyouji Hayashi, Takuya Numasawa, Seiko Harata, Kazunori Yone, Shunji Matsunaga, Brith Otterud, Ituro Inoue, and Mark Leppert

1468 Haplotype Mapping of a Major Quantitative-Trait Locus for Fetal Hemoglobin Production, on Chromosome 6q23
C. Garner, J. Mitchell, T. Hatzis, J. Reittie, M. Farrall, and S. L. Thein

1475 An Alternative Route for Multistep Tumorigenesis in a Novel Case of Hereditary Renal Cell Cancer and a t(2;3)(q35;q21) Chromosome Translocation
Daniëlle Bodmer, Marc J. Eleveld, Marjolijn I. L. Ligtenberg, Marian A. J. Weterman, Bert A. P. Janssen, Dominique F. C. M. Smeets, Peter E. J. de Wit, Anke van den Berg, Eva van den Berg, Marianne I. Koolen, and Ad Geurts van Kessel

1484 Genetic Analysis of Meiotic Recombination in Humans by Use of Sperm Typing: Reduced Recombination within a Heterozygous Paracentric Inversion of Chromosome 9q32-q34.3
Graeme M. Brown, Margaret Leversha, Maj Hulten, Malcolm A. Ferguson-Smith, Nabeel A. Affara, and Robert A. Furlong

1493 Parental Origin–Dependent, Male Offspring–Specific Transmission-Ratio Distortion at Loci on the Human X Chromosome
A. K. Naumova, M. Leppert, D. F. Barker, K. Morgan, and C. Sapienza

1500 Identification of Cryptic Rearrangements in Patients with 18q− Deletion Syndrome
Zoran Brkanac, Jannine D. Cody, Robin J. Leach, and Barbara R. DuPont

1507 Dating the Origin of the *CCR5*-Δ*32* AIDS-Resistance Allele by the Coalescence of Haplotypes
J. Claiborne Stephens, David E. Reich, David B. Goldstein, Hyoung Doo Shin, Michael W. Smith, Mary Carrington, Cheryl Winkler, Gavin A. Huttley, Rando Allikmets, Lynn Schriml, Bernard Gerrard, Michael Malasky, Maria D. Ramos, Susanne Morlot, Maria Tzetis, Carole Oddoux, Francesco S. di Giovine, Georgios Nasioulas, David Chandler, Michael Aseev, Matthew Hanson, Luba Kalaydjieva, Damjan Glavac, Paolo Gasparini, E. Kanavakis, Mireille Claustres, Marios Kambouris, Harry Ostrer, Gordon Duff, Vladislav Baranov, Hiljar Sibul, Andres Metspalu, David Goldman, Nick Martin, David Duffy, Jorg Schmidtke, Xavier Estivill, Stephen J. O'Brien, and Michael Dean

1516 Missense Mutations in Disease Genes: A Bayesian Approach to Evaluate Causality
Gloria M. Petersen, Giovanni Parmigiani, and Duncan Thomas

1525 A Model for Antagonistic Pleiotropic Gene Action for Mortality and Advanced Age
Bruno Toupance, Bernard Godelle, Pierre-Henri Gouyon, and François Schächter

Letters to the Editor

1535 Phosphomannose Isomerase Deficiency: A Carbohydrate-Deficient Glycoprotein Syndrome with Hepatic-Intestinal Presentation
Jaak Jaeken, Gert Matthijs, Jean-Marie Saudubray, Carlo Dionisi-Vici, Enrico Bertini, Pascale de Lonlay, Hugues Henri, Hubert Carchon, Els Schollen, and Emile Van Schaftingen

1539 Temperature-Sensitive Phenotypes of Peroxisome-Assembly Processes Represent the Milder Forms of Human Peroxisome-Biogenesis Disorders
Atsushi Imamura, Toshiro Tsukamoto, Nobuyuki Shimozawa, Yasuyuki Suzuki, Zhonghi Zhang, Tsuneo Imanaka, Yukio Fujiki, Tadao Orii, Naomi Kondo, and Takashi Osumi

1543 A Breast Cancer Patient of Scottish Descent with Germ-Line Mutations in *BRCA1* and *BRCA2*
Alexander Liede, Pauline Rehal, Danny Vesprini, Elaine Jack, John Abrahamson, and Steven A. Narod

1544 Evidence of Founder Mutations in Finnish BRCA1 and BRCA2 Families
Pia Huusko, Kati Pääkkönen, Virpi Launonen, Minna Pöyhönen, Guillermo Blanco, Antti Kauppila, Ulla Puistola, Heikki Kiviniemi, Marika Kujala, Jaakko Leisti, and Robert Winqvist

1548 A Triplet Repeat on 17q Accounts for Most Expansions Detected by the Repeat-Expansion–Detection Technique
Ellen Sidransky, Catherine Burgess, Takeshi Ikeuchi, Kerstin Lindblad, Robert T. Long, Robert A. Philibert, Judith Rapoport, Martin Schalling, Shoji Tsuji, and Edward I. Ginns

1551 Paternal Isodisomy of Chromosome 7 Associated with Complete Situs Inversus and Immotile Cilia
Yanzhen Pan, Christopher D. McCaskill, Katherine H. Thompson, John Hicks, Brett Casey, Lisa G. Shaffer, and William J. Craigen

1555 Familial Skewed X Inactivation and X-Linked Mutations: Unbalanced X Inactivation is a Powerful Means to Ascertain X-Linked Genes That Affect Cell Proliferation
Barbara R. Migeon and Camille Haisley-Royster

1557 Reply to Migeon and Haisley-Royster
Eric Hoffman, Elena Pegoraro, and Mark Lanasa

1558 Difficulties in the Estimation of Ethnic Affiliation
Charles H. Brenner

1560 Reply to Brenner
Mark D. Shriver, Michael W. Smith, and Li Jin

1561 **Discriminating between True and False-Positive Peaks in a Genomewide Linkage Scan, by Use of the Peak Length**
Michael Knapp

Announcements

1563 **Employment and Fellowship Opportunities; WWW Cell Culture Catalog; Conference**

1565 **Author Index for Volume 62**

1575 **Subject Index for Volume 62**

1587 **Contents of Volume 62**

Information for Contributors